Assessment of patients with seizures

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In this series, we present authoritative advice on the investigation of a common clinical problem, specially commissioned for family doctors by the Board of Continuing Medical Education of the Royal Australasian College of Physicians.

Seizures are a common phenomenon, with about 5% of people suffering an epileptic seizure at some time in their lives.[1] The busy general practitioner will see patients presenting with their first ever epileptic or nonepileptic seizure as well as patients with epilepsy (recurrent unprovoked epileptic seizures) presenting with breakthrough seizures. This article discusses the key issues that should be addressed in the diagnostic evaluation of these patients.

Is it an epileptic seizure?

It is important to consider nonepileptic paroxysmal disorders in the differential diagnosis. Syncope is often incorrectly diagnosed as an epileptic seizure. The patient is almost always erect (sitting or standing) before syncope and may recall a sense of lightheadedness or dizziness followed by visual impairment, distorted hearing and loss of muscle tone immediately preceding collapse. Stiffening, jerking of the limbs and even brief tonic–clonic movements are observed in up to 90% of syncope cases.[2] Loss of consciousness is brief – seconds rather than minutes – and postictal confusion is not observed (Table 1). Patients can usually recall regaining consciousness where they collapsed and their companions fussing over them. Contrast this with the recovery from a tonic–clonic seizure, when the patient collapses and next recalls the ambulance officers or the emergency department staff.

Syncope in association with postural change would suggest orthostatic syncope. Knowledge of the patient's lying and standing blood pressures may be helpful if this is suspected, and a tilt table test may be required to support the diagnosis. Cardiac arrhythmia may also present as syncope, so all patients with syncope should have an electrocardiogram.[3]

Other mimics of epileptic seizures should also

IN SUMMARY

- **Many patients presenting for the first time with a seizure have had previous nonconvulsive seizures and have epilepsy.**
- **Never assume a diagnosis of epileptic seizure without a supporting history because several nonepileptic disorders, including syncope and pseudoseizures, may mimic epileptic seizures.**
- **Electroencephalography (EEG) is an important diagnostic test for patients presenting with seizures; the presence of interictal epileptiform discharges on EEG strongly supports a diagnosis of epileptic seizures.**
- **Computed tomography is useful only in the acute setting when looking for structural lesions such as a stroke, abscess, haematoma or tumour.**
- **Partial seizures and evidence of neurological dysfunction are predictive of seizure recurrence.**

continued

Table 1. Differentiating syncope from tonic–clonic seizures

Clinical factor	Syncope	Tonic–clonic seizures
Precipitating factors	Erect posture, warm environment, fright or pain	Usually none but sleep deprivation may be contributory
Prodrome	Lightheaded, dizzy, queasy, dimming vision, loss of colour, 'grey out'	May have an aura
Occurrence in sleep	Never	Common
Evolution	Limp fall, likely to be motionless, pallor, clammy skin. May have tonic phase with generalised stiffening and few jerks. May be averted by head down or recumbency	Sudden loss of consciousness, likely to have increased tone, massive truncal flexion or extension followed by synchronous jerking of body and limbs with rubor or cyanosis and sweating, likely to be unconsciousness
Skin	Pale and cool	Flushed, cyanosed and warm
Incontinence	Rare	Not uncommon
Self-injury	Rare	Common
Duration of loss consciousness	20 to 60 seconds	2 to 5 minutes
Postictal confusion	Minimal	Marked

Table 2. Mimics of epileptic seizures

Seizures characterised by collapse with or without stiffening and jerking

- Syncope
- Pseudoseizures
- Vertebrobasilar transient ischaemic attack
- Metabolic disorders
  - Hypoglycaemia
  - Hypoadrenalism
- Paroxysmal movement disorders
- Drug and alcohol abuse
- Cataplexy

Seizures characterised by non-convulsive confusion or agitation

- Migraine
- Hypoglycaemia
- Anxiety disorders or panic attacks
- Transient global amnesia
- Parasomnias

be considered, especially in children.[4] These seizures can be divided into two categories, characterised either by unresponsiveness, collapse, stiffening and jerking movements or by a lack of pronounced motor activity (Table 2). Pseudoseizures are episodic behavioural events with sensory or motor phenomenon that resemble epileptic seizures (Table 3). They have a psychological basis and can be explained as an episodic dissociation in the setting of subconscious stress. Events confined to sleep are more likely to be parasomnias than seizures, especially when they occur in children. Patients with paroxysmal movement disorders do not show confusion or loss of awareness. Children with episodic unresponsiveness may be experiencing complex partial seizures, absence seizures or nonepileptic daydreaming (Table 4): suspect nonepileptic daydreaming in children with learning disorders when their teacher first reports the events.

Is it the first seizure?

Up to 74% of patients with 'newly identified unprovoked seizures' have experienced previous seizures before the first medical contact.[5] Absence seizures, auras (simple partial seizures) and myoclonic jerks may be ignored or go unnoticed for years before medical attention is sought. A patient presenting with a tonic–clonic seizure and previous partial seizures has a greater than 80% risk of further seizures.

Did the seizure have a partial or generalised onset?

Patients with partial seizures of recent onset demand detailed investigation with neuroimaging studies. Such patients may experience warning symptoms: the so-called 'aura'. An aura is a simple partial seizure and indicates a focal onset. A simple partial seizure occurs when the patient experiences the symptoms of a seizure without a loss of awareness. Often patients find the symptoms strange and difficult to describe, so ask them if the episodes are stereotyped, whether they occur sometimes without confusion, and whether the episodes wake them from sleep.

Generalised seizures (absence, myoclonic or tonic–clonic seizures) are not preceded by auras since they involve the whole brain at onset. Do not assume a tonic–clonic seizure has a generalised onset just because the patient has no recollection of the onset. Witness accounts of the onset of the seizure are always valuable. Witnesses to partial seizures may describe the patient having a sudden behavioural change followed by automatisms, oral (lip smacking or chewing) and manual (patting and fiddling), accompanied by restlessness preceding the development of a tonic–clonic seizure. Forced head turning occurring before a patient progresses to a secondary generalised tonic–clonic seizure indicates a partial seizure arising in the contralateral hemisphere. Postictal hemiparesis (Todd's paresis) occurs contralateral to the hemisphere of focal onset. Partial seizures are predictive of seizure recurrence.

Were there any precipitants?

Seizures may be provoked by recreational drugs, alcohol, sleep deprivation, metabolic derangement, acute brain insults and some prescribed medications (Table 5). In young children, febrile illness is the most common cause of acute symptomatic seizures. In those patients with epilepsy presenting with breakthrough seizures, a search for missed medication doses, medication interactions or intercurrent illness is usually rewarding.

Is there any underlying neurological dysfunction?

Past medical history of perinatal insults, developmental delay, CNS infections or head trauma suggests a possible underlying cerebral pathology. The general physical examination should include a search for signs of systemic illness, for the skin stigmata that characterise neurocutaneous disorders such

Table 3. Differential diagnosis of psychogenic seizures

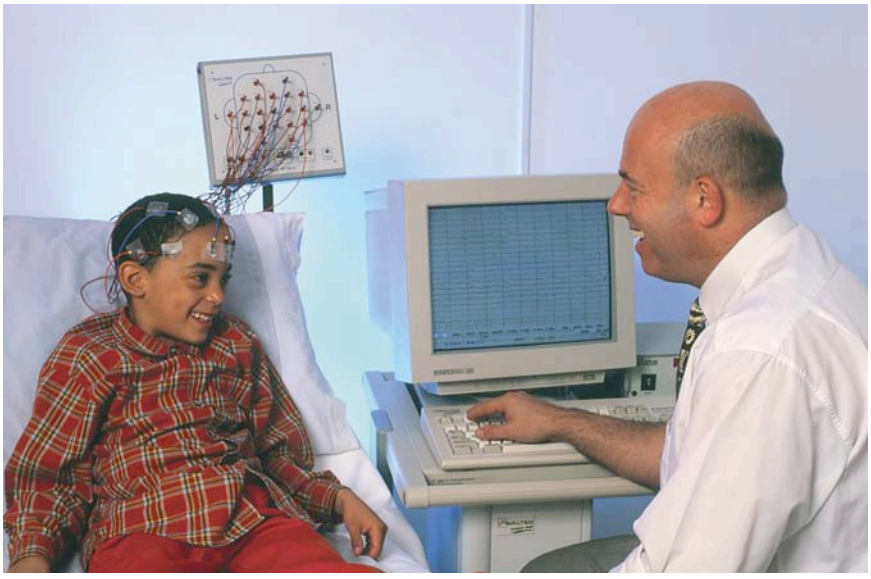
Clinical factor	Psychogenic seizures	Epileptic seizures
Age at onset	Usually occur in patients who are older than 8 to 10 years and usually in females (15 to 30% of cases are in males)	Any age and no sex predominance
Duration of seizures	May be very prolonged	Usually seconds to minutes
Evolution	May have a gradual onset and ending	Usually an abrupt onset
Quality of convulsive movements	Thrashing, asynchronous limb movements, often with partial responsiveness. Movements may wax and wane during the episode	Usually rhythmical and synchronous with loss of consciousness
Stereotypic attacks	No	Yes
Examination during the seizure	May resist examination, combative	Usually unresponsive and amnestic for ictal events
Self-injury	Rare	Common in generalised tonic–clonic seizures
Incontinence	Rare	Common in generalised tonic–clonic seizures
Occurrence during sleep	No, may be nocturnal but occur while awake	Common
Changes in seizure frequency with medication	Rare	Usual
Interictal EEG	Repeatedly normal	Often abnormal
Ictal EEG	No EEG seizure patterns, normal rhythms while unresponsive	EEG seizure patterns
Pitfalls in diagnosis	• Psychological factors may not be immediately apparent • Misleading information may be given by parents (Munchausen by proxy)	• Asynchronous vigorous automatisms are found in frontal lobe seizures • Bilateral limb posturing without loss of consciousness occurs in supplementary motor seizures • EEG seizure patterns may be absent during some simple partial seizures

continued

Table 4. Differential diagnosis of episodic unresponsiveness in children without convulsions

Clinical factor	Absence seizures	Staring, inattention
Frequency	Multiple, daily	Daily, situational – e.g. may only occur at school
Duration	Often less than 10 seconds and rarely greater than 30 seconds	Seconds to minutes
Aura	Not present	Not present
Abrupt interruption of child's activity	Yes – e.g. speech arrest midsentence, pauses while eating, playing or fighting	Activities such as play or eating are not abruptly interrupted, no sudden onset
Eyelid flutter	Common, often with upward eye movement	Not present
Myoclonic jerks	Common	Not present
Automatisms	Occur when absence seizures are prolonged, usually mild	Not present
Responsiveness of patient	Unresponsive	Responds to touch
Postictal impairment	None	No
EEG	Generalised 3 Hz spike and wave complexes	Normal
First line medication	Sodium valproate, ethosuximide	None

as tuberous sclerosis or Sturge–Weber syndrome, and for signs of head trauma and illicit drug use. However, these examinations rarely yield positive findings. A careful neurological examination may reveal evidence of an underlying cerebral pathology such as limb asymmetry, which possibly suggests an early brain injury or malformation of cortical development. Evidence of underlying neurological dysfunction is predictive of seizure recurrence.



PHOTOLIBRARY

Figure 1. A child undergoing EEG, an important diagnostic test for patients presenting with seizures.

What investigations are required?

Initial laboratory investigations, such as serum biochemistry and glucose and liver function tests, may identify an underlying cause for the seizures and direct the physician to undertake a more detailed metabolic screening. However, routine biochemistry and haematology tests after a patient presents to the accident and emergency department rarely reveal anything of value.[6] A urine drug screen is important in adolescents and adults. For patients already being treated for epilepsy, measurement of the serum levels of their antiepileptic drugs is a useful way to assess medication compliance. Initiate a lumbar puncture if there is any suspicion of meningitis or encephalitis.

Electroencephalography (EEG) is an important diagnostic test for patients presenting with seizures (Figure 1). The presence of interictal epileptiform discharges strongly supports a diagnosis of epileptic seizures rather than nonepileptic seizures and contributes greatly to the diagnosis of specific epileptic syndromes.

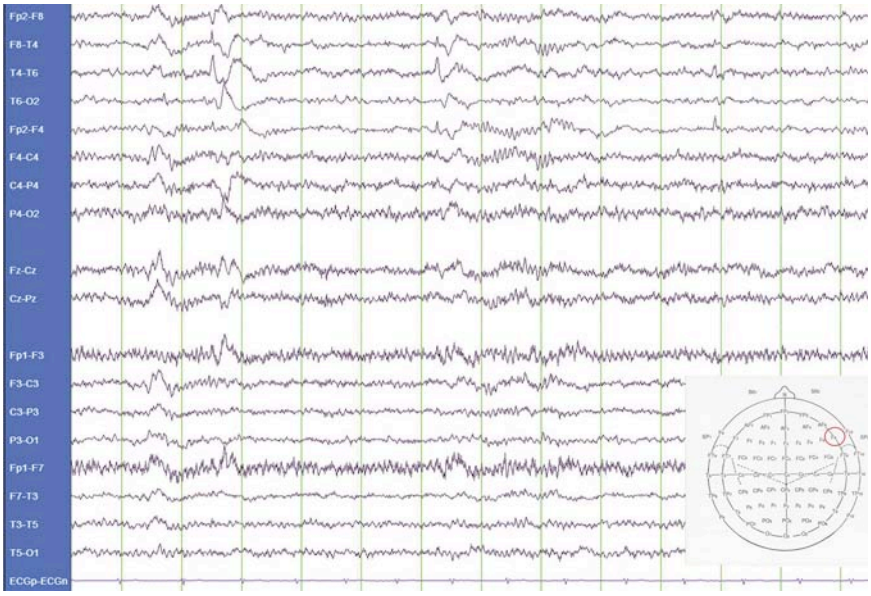


Figure 2. An electroencephalogram showing focal epileptiform discharges in the right frontotemporal electrodes. The discharge maxima is shown in the insert electrode F8. These findings provide support for a diagnosis of partial seizures.

Focal abnormalities, slowing or spikes suggest a focal onset for the seizures and direct the search towards an underlying structural pathology. Epileptiform discharges on EEG after presentation of a first ever seizure are strong predictors of seizure recurrence. However, EEG is not a particularly sensitive tool: only 30 to 50% of patients who present following an epileptic seizure will have epileptiform discharges on EEG (Figure 2). Better results are obtained if EEG is performed within 24 hours of the seizure[7] and following partial sleep deprivation.[8] If the EEG is normal but suspicion of epilepsy is high, repeat EEGs should be conducted. However, normal EEGs during wakefulness and sleep do not rule out a diagnosis of epileptic seizures.

It is only helpful to use computed tomography (CT) in the acute setting, when structural lesions such as a stroke, abscess, haematoma or tumour are sought. A CT scan is imperative for patients who are still confused or unconsciousness after 30 to 60 minutes, have a history of recent head trauma or an abnormal postictal neurological examination, or present with status epilepticus. A CT scan is not an adequate investigation for a patient presenting with partial seizures. The structural neuroimaging of choice in this case is magnetic resonance imaging (MRI) as it provides the best definition of normal and abnormal structures in the brain. It also enables identification of the more subtle pathologies that underlie partial seizures, such as malformations of cortical development and mesial temporal sclerosis. All patients with new-onset partial seizures should have MRI to exclude structural abnormalities.

What are the chances of seizure recurrence?

For patients presenting with their first seizure, there is a 50% overall risk that they will experience a second seizure in the next 12 months; however, most of the seizure recurrences will occur in the next three months.[9] There is a 60 to 70% chance of a seizure recurring in the next 12 months if the patient presents with unprovoked seizures of partial onset, there is evidence of underlying neurological dysfunction, or the patient has an abnormal EEG or a structural lesion on MRI/CT. This group is most likely to be presenting with their first seizure of epilepsy and should be advised to consider antiepileptic medication. Conversely, patients whose seizures seem to be a result of a stimulus and who do not have an underlying cerebral pathology or abnormal EEG or radiological tests, have a less than 40% chance of experiencing recurrent seizures if they are able to avoid the provocative stimulus. Patients presenting for the first time who have a history of previous nonconvulsive seizures have epilepsy.

Table 5. Medications that may provoke seizures or lower seizure threshold

Analgesics – e.g. tramadol, diamorphine, lignocaine, pethidine
Antibiotics – e.g. penicillins cephalosporins, isoniazid, quinolones
Antidepressants – e.g. selective serotonin reuptake inhibitors, tricyclic antidepressants (overdose)
Antihistamines (overdose)
Antimalarials – e.g. chloroquine
Antipsychotics – particularly clozapine and lithium (may be prescribed as antiemetics)
Amphetamines
Baclofen
Bupropion
Chemotherapy medications – e.g. vincristine, cyclosporin, mitozantrone, isotretinoin
Oral contraceptives (as interact with antiepileptic medication)
Theophylline
Traditional Chinese and Indian medicines

Should antiepileptic medication be started?

The choice of antiepileptic medication depends not only on efficacy, but also on safety and possible long term side effects. In females, potential fetal teratogenic effects should be discussed as well as the risk of osteoporosis if the epilepsy is chronic. Generally, it is the type of seizure that dictates the choice of therapy. Carbamazepine (Tegretol, Teril) is recommended for partial epilepsies and sodium valproate (Epilim, Valpro) for generalised epilepsies as the efficacy of these medications is as good as that of the newer agents.[10,11] Ethosuximide (Zarontin) is an appropriate drug for patients with absence seizures, but it does not control complex partial or tonic–clonic seizures.[12] Lamotrigine, topiramate (Topamax) and oxcarbazepine (Trileptal) should be considered as add-on therapy. Other newer adjunctive antiepileptic medication levetiracetam (Keppra) and gabapentin are notable for their renal clearance rather than hepatic metabolism. Phenytoin (Dilantin, Phenytoin Injection) is still an excellent choice for partial and generalised seizures in an acute setting.

What precautions should patients take?

Recommended safety precautions should be sensible and relevant to the particular person involved. Advise patients to avoid high risk activities such as driving, extreme sports, surfing, unsupervised swimming, and climbing to heights greater than their own for at least three to six months after an unprovoked seizure. The duration of these advised precautions depends on the likelihood of seizure recurrence and on the treatment strategy. In an adult presenting with his or her first ever seizure in whom antiepileptic medication is not initiated, a six month seizure-free period is advised before allowing the patient to drive. This can be reduced to a three-month period free of seizures if the patient starts antiepileptic medication. In patients with chronic epilepsy (i.e. a history of previously uncontrolled seizures), a seizure-free period of one to two years is required, depending on specific circumstances.

Useful resources for patients

The effect on patients and their families following the first occurrence of an epileptic seizure can be profound. The more a person understands about his or her seizures and epilepsy, the less frightening the future will be. Helpful information can be gained from the following two educational resources:

- Epilepsy Action: www.epilepsy.org.au (telephone: 1300 374 537)
- Epilepsy Australia: www.epilepsyaustralia.org (telephone: 1300 852 853).

Conclusion

Never assume a diagnosis of epileptic seizure in a patient without a supporting history as nonepileptic disorders may mimic epileptic seizures. An accurate clinical history from a witness is the most important complement to the patient's own history. Few investigations provide conclusive diagnostic results, and the assessment is largely clinical. The clinician should try to determine the cause of the seizure and the likelihood of a recurrence when planning the management of a patient's seizures. Many patients presenting for the first time have had previous non-convulsive seizures and have epilepsy. Seizure type and evidence of neurological dysfunction are strong predictors of seizure recurrence. MT

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